(Reprinted from Nature, Vol. 198, No. 4879, pp. 428–429, May 4, 1963)

MOLECULAR BIOLOGY, EUGENICS AND EUPHENICS*

By Prof. JOSHUA LEDERBERG

Kennedy Laboratories for Molecular Medicine, Department of Genetics, School of Medicine, Stanford University, Palo Alto, California

THE risks of scientific prophecy are well known. But foresight about our scientific culture is as important for the culture to gather as it is difficult for the scientist to expound. His credentials to speak on the impact of science on human welfare are scarcely unique, but he does have a responsibility which stems from his technical judgment of the plausibility and especially the time-scale of scientific advance, which by furthering human power must impinge on policy.

Recent years have seen breath-taking advances in the molecular foundations of biology, at a pace that reminds us that the gross effort in science in one year now matches the total accumulation to the beginning of this century; as much scientific effort has been invested since 1950 as was in all previous history. These actuarial calculations cannot, of course, measure the intellectual value of the return, nor do they take account either of instrumentation multipliers or of the overloading of the communications net. The details of these advances are well told elsewhere. What must be noted here is the solution to the fundamental problems of genetics: the encoding of genetic information in the structure of DNA, and the enzymatic mechanism by which the nucleotide sequence is replicated. Intertwined with these developments have been the unification of terrestrial biology within a single biochemical genetic scheme, and the now rapid unravelling of the cellular mechanism of protein synthesis whereby the genetic information is translated into the working machinery of life.

Eugenics, the conscious betterment of man's genetic quality, has fascinated many idealistic thinkers. Like other noble aims it has been perverted to justify unthinkable inhumanity; which does not help to assess its validity and feasibility by ethically proper means. The case for eugenics, ably presented by Huxley and by Muller, has one most trenchant argument against complacency: man's long pre-cultural evolution has given him a biological legacy which can be only fortuitously

* Substance of an address to the Symposium on "The Future of Man" held at the Ciba Foundation, London, November 26–30, 1962. The full proceedings of the Symposium will be published by Messrs. J. and A. Churchill, Ltd.

adapted to the physical power and technological complexity of the modern world. In a word, man, unless he grows less 'human', may destroy himself.

Eugenic progress creeps within the joint constraints of our limited knowledge of human genetics and customary wisdom concerning its implementation. Even so, the eugenicists argue, some beginning must be made, to offset exigent counter-eugenic influences, perhaps to assure that some eugenic wisdom survives until the species can or must act.

The new biology is relevant here—ultimately it could diagnose, then specify, the actual DNA composition of ideal man. But clearly, this will not happen for some time ("if ever", most of my colleagues will reassure themselves, while they concentrate on more penetrating assaults on these secrets).

Having shared this view, I may record how easy and tempting it is to postpone consideration of the probable impact of biological knowledge on human affairs. It is difficult enough to make a fragmentary contribution to such knowledge, much more to be usefully concerned with its total consequences.

The emphasis on eugenics as the point of application of molecular biology overlooks the most immediate prospects for the understanding and then control of human development. To dramatize the antinomy, I propose the term 'euphenics' as the counterpart of 'eugenics', in the same sense that 'phenotype' is opposed to 'genotype'.

Development is the translation of the genetic instructions of the egg, embodied in its DNA, to direct the unfolding of its substance to form the adult organism in all its aspects, which comprise its phenotype. The crucial problem of embryology is the regulation and execution of protein synthesis, how some DNA segments are made to call out their instructions, others suppressed, which underlies the orderly differentiation of cell types.

Until now, the major problems of human development —not only embryology, but also the phenomena of learning (in its neurobiological aspects), immunity (with its bearing on transplantation), neoplasia and senescence— could be approached at only the most superficial level. They are about to be transformed in the sense that genetics has been, as epiphenomena of protein and nucleic acid synthesis. The present intensity of effort suggests a span of from five to no more than twenty years for an analogous systematization.

On these premises it would be incredible if we did not have the basis of developmental engineering technique, for example, to regulate the size of the human brain by prenatal or early postnatal intervention.

The basic concept of molecular biology is the chain of information from DNA to RNA to protein. We are just now beginning to ask questions of mental mechanism from

this point of view. The simplest and one of the oldest of speculations about memory is the modification of neuronal interconnexion through control of synthesis and deposition of durable proteins at the interfaces. A plausible link between electrical impulses and protein synthesis might be the accompanying shifts of potassium and sodium concentrations; these ions being also important cofactors for several enzymes involved in protein synthesis. Thus, cation balance could control the assembly of chosen polypeptide chains into a complex protein, the selective reactions of glutamine —$CONH_2$ in protein, or the imperfect specifications of degenerate RNA codes. Such speculations merely illustrate the relationship of mental science to molecular biology.

In another field of developmental engineering Medawar has already exhibited a *tour de force*, the abolition of immunity to transplants introduced in early life, which has clarified the biology of immunity and points to the solution of the transplantation problem. At present, human individuality is the bar to spare-part medicine: the organism rejects grafts from other individuals even of the same species, the alien tissue a life-extending kidney or heart notwithstanding. The solution to the homograft problem now partly resolved must be imminent, under intensive attack as an aspect of the cell biology of immunity, and of the molecular structure and cytosynthesis of antibodies and tissue antigens. The management of the problems and opportunities it raises should be a prototype for the exercise of responsible power in biological engineering. There is no evident forethought of them, perhaps just because of their cataclysmic impact on medicine.

What if surgical finesse were now the only criterion of transplantability ? The direct replacement of defective, diseased or worn-out organs could pre-empt all available surgical talent for years to come. Then, many potent régimes, once restrained by the side-effects on other organs, are now available to internal medicine. These tools, like present-day drugs, will also have an indispensable role in the treatment of healthy individuals.

The most nightmarish prospects arise from indifference to technological and procedural requirements with respect to the sources of indispensable, scarce life-saving organs. The orderly evolution of transplantation technique might be facilitated if organ transplants in man (with evident trivial exceptions) were already subject to formal registration as vital statistics.

Many social problems arise from technological imbalance, or at least have possible technological antidotes which can then be properly discussed here. For example, the political stability of the world might be enhanced if the present technology of the detection matched that of the power output of nuclear explosives; likewise for the

moderation of human prolificity concurrently with infant mortality. In the present case intolerable stresses arising from the economics of human organs could be averted by further advances beyond the first stage of successful homotransplantation. These might include a eugenic programme on other species to facilitate their use as sources of organs. The more difficult problem of heterotransplantation, from other species, would be mitigated if these sources were genetically uniform and could be specifically selected for immunological and functional suitability. At present the only animals which begin to fit these criteria are inbred mice. The industrial manufacture of specific proteins (either by chemical- or cytosynthesis) would be an invaluable adjunct. Such precious proteins, for example, hormones or enzymes, are sometimes the functional purpose of a transplant. As antibodies or tissue antigens they would play a specific part in neutralizing the homograft rejection mechanism. As structural proteins they would be valuable for the manufacture of compatible parts and connexions.

The heart probably poses the most perplexing problems of supply and allocation. Yet, of all the vital organs, this should be the first to be simulated by a mechanical analogue—machines are already available for short-term use during surgery. Should the engineering effort be accelerated to produce a practical substitute for this efficient pump? These proposals stress engineering development, partly to illustrate a prevalent gap between academic science and its useful implementation in this aspect of human welfare. There are many equally insistent candidates for the succession to military uses of industrial technology.

Man's control of his own development, 'euphenics', transmutes the means, and also the ends of eugenics, as have all the precedent cultural revolutions that have shaped the species: language, agriculture, political organization, the physical technologies. Eugenics is aimed at the design of a reaction system (a DNA sequence) that, in a given context, will develop to a somehow defined goal. Few insights would be worth more than the design of human value—but will culture stand still merely to validate the eugenic criteria of a past generation? For a given end, the means will have shifted: the best inborn pattern for normal development will not always react best to euphenic control.

Within the framework of formal eugenics the disruptive effects of recombination may need further investigation. Most genes segregate independently of sex, but must then work in concert with the bio-cultural dimorphism of sex. This must impede stringent selection; or conversely, does rapid eugenics not imply the convergence of the sexes to a common goal? At a considerable cost in its rate the evolutionary process might be

confined to sex-limited, -linked, or -irrelevant mutations, if any, which still affect personality. Euphenics can switch the entire programme to match the sexual or other role-defining polymorphisms. Education—the whole cultural apparatus—does this now.

Euphenics will, of course, open the way for a more comprehensive eugenics, if only through the systematization of knowledge of gene action. Even now the outlook for eugenic improvement of intelligence would be improved by a biochemical assay for it.

In our inquiry on his future, the aims of human existence are inseparable from the power and responsibility for human nature. It becomes more perplexing as biological technology dissolves the barriers around individual man and intrudes on his secret, germinal continuity. The humanist premise of individual value must face the issue of a definition of man, taking full account of his psychosocial progeny. We now recognize genetic continuity in mechanistic terms as a nucleotide sequence—in due course this will itself be subordinate to the psychosocial machinery. While man perfects the knowledge of his own mechanism, he also vitalizes machines on to a convergent evolutionary pathway. Genetics is rapidly becoming a corollary of information theory. As he thus evolves from substance to concept, Is it the bond of genetics or of communication that qualifies 'man' for the aspirations of humanistic fulfilment, apart from the other robots born of human thought ?

Printed in Great Britain by Fisher, Knight & Co., Ltd., St. Albans.